REMARKS

Status of the Claims

Claims 1, 4 and 6-9 are pending. Claims 2, 3 and 5 have been cancelled without prejudice or disclaimer of the subject matter claimed therein.

Claims 1, 4, and 6 have been amended. Representative support for the amendments to the claims 1, 4, and 6 can be found in claims 1, 4, and 6 as originally filed.

Claims 7-9 have been added. Representative support for claims 7 and 8 can be found in examples 4 and 5 respectively. Representative support for claim 9 can be found on page 2, lines 21-24.

Applicants submit that the amendments to the claims and the addition of the new claims do not introduce new matter.

Applicants reserve the right to pursue the subject matter deleted from the pending claims or in the deleted claims in one or more divisional and/or continuation applications.

Objections to the Specification

The Office Action objected to the specification for failing to capitalize trademarks and failing to provide generic terminology. Applicants have amended the specification to capitalize the trademarks used in the present application. Applicants submit that TOXOVAX does not have a generic name and has been otherwise adequately described in the paragraph beginning on page 2, line 32 to protect its validity as a trademark.

Rejection of Claims Under 35 U.S.C. § 101

Claims 4 and 5 are rejected under 35 U.S.C. § 101 as allegedly not being supported by a well established utility. Claim 4 has been amended and claim 5 has been cancelled without prejudice or disclaimer of the subject matter claimed therein. Claim 4 has been amended to recite a positive step as suggested by the office action.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

Claim 6 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

The claims allegedly contain subject matter which was not described in the specification in a way as to enable one skilled in the art to make and/or use the invention.

The Office Action suggests that the application as filed discloses data only for a *Toxoplasma gondii* strain, and therefore does not enable a vaccine comprising a mutant strain from any species of an Apicomplex family of Sarcocystidae. Without acquiescing to the propriety of the rejection, Applicant has amended the claims to recite a mutant strain of *Toxoplasma gondii* in the interest of expediting allowance of the application. Applicants submit that this rejection has been overcome.

The Office Action alleges that the data included in the application does not demonstrate that the composition confers protection against infection with Toxoplasma gondii. However, the Office Action acknowledges that the application shows that mice immunized with the *Toxoplasma gondii* mutant, comprising inactivated MIC1 and MIC3 ("mic1-3 KO"), are protected with a rate of 99% against brain cyst formation during a reinfection with the *Toxoplasma gondii* strain 76K (see page 5, lines 7 to 10 of the Office Action). In addition, the Office Action acknowledges that the application discloses that the rate of febrile abortions decreased for ewes immunized with mic1-3 KO before being infected with oocysts of *Toxoplasma gondii* and that the present application complies with the enablement requirement with regard to the reduction of febrile abortions caused by *T. gondii* through the administration of the mic1-3KO mutant strain.

Applicants respectfully point out that the present application does show a challenge experiment which demonstrates protection against infection. Applicants submit that Example 4, on page 23, lines 25 to 28, discloses that "21 mice (batch 2) received the mic1-3 KO mutant and were then reinfected approximately 1 month later with cystogenic *Toxoplasma gondii* strain 76." Here, the immunization step is the administration of mic1-3 KO mutant and the challenge step is the latter infection with *Toxoplasma gondii* strain 76K. The mice immunized with the mic1-3KO mutant formed virtually no brain cysts during the re-infection with the *Toxoplasma gondii* strain 76K (page 26, lines 8-15).

Similarly, the experiments that were performed on ewes consisted of i) immunizing two batches of ewes, one of these batches with a low dose and the other batch with a high dose of mic1-3KO tachyzoites and ii) infecting the gestating ewes by feeding them with 400 oocysts of

Toxoplasma gondii (see Example 5 on page 28, lines 10 to 12 and page 30, lines 19 to 24). Thus, the application as filed shows the reduction of febrile abortions (abortions which occur following the thermal peak following the infection) caused by *Toxoplasma gondii* through the administration of mic1-3 KO mutant strain. Moreover, the application demonstrates that the administration of mic1-3 KO mutant strain also reduces the rate of abortions due to the infection of the fetus with *Toxoplasma gondii* (see Table II on page 33 and Table V on page 37).

In both of these challenge experiments, the protective effect noticed after the administration of the mic1-3 KO mutant strain demonstrates that a *Toxoplasma gondii* strain comprising inactivated adhesins MIC1 and MIC3 elicits a protective immune response against a latter *Toxoplasma gondii* infection.

The Office Action alleges that page 37 of the application shows zero protection against *Toxoplasma gondii* and does not demonstrate that the claimed composition confers protection against infection by *Toxoplasma gondii*. Applicants respectfully point out that Table VI, on page 37 of the application, which summarizes the results obtained with gestating ewes vaccinated with a mic1-3 KO mutant strain, indicates that vaccination with mic1-3 KO mutant strain, named ToxoKO in Table VI, induces a protection of 66.6%. This level of protection is similar to the level of protection conferred by administration of *Toxoplasma gondii* S48 strain, which is the *Toxoplasma gondii* strain used in the only anti-toxoplasmosis vaccine commercially available (TOXOVAX®). Applicants also point out that there is zero protection only with the control batch of 12 ewes, i.e. the ewes which are not immunized before being challenged with *Toxoplasma gondii*.

Applicants submit that the present application clearly demonstrates that a *Toxoplasma gondii* strain, wherein the adhesins MIC1 and MIC3 are inactivated does have a protective effect against later *Toxoplasma gondii* infection. Moreover, the level of protection conferred by this strain is similar to the level of protection which is conferred by the anti-toxoplasmosis vaccine currently available.

Applicants have considered each of the Wands factors. In view of the reasons set forth above, the application provides sufficient evidence and examples to enable one having ordinary skill in the art to practice the claimed invention without undue burden.

Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

Claims 1-5 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite for allegedly failing to point out and distinctly claim the subject matter which the applicant regards as the invention.

Applicants submit that this rejection is moot because claims 1-3 have been amended, and because claim 4 has been amended to recite a method step.

Rejection of Claims Under 35 U.S.C. § 103

Claims 1-3 are rejected under 35 U.S.C. § 103 as obvious over Bassuny *et al.* ("*Bassuny"*) in view of Meissner *et al.* ("Meissner").

The Office Action states that Bassuny discloses a mutant strain of *Toxoplasma gondii* comprising a plasmid encoding an immature form of MIC3 and that it would have been obvious to incorporate the mutant strain disclosed by Meissner with the mutant strain disclosed by Bassuny to obtain the mutant strain of the present invention.

Applicants submit that Bassuny is directed to DNA vaccination against toxoplasmosis which is performed by administrating a plasmid encoding an immature form of MIC3 protein (pMIC3i) to a mouse. In contrast, the present invention employs a totally different approach consisting of using a mutant strain of *Toxoplasma gondii*. Further, Bassuny does not disclose a *Toxoplasma gondii* mutant strain and in particular, it does not disclose a *Toxoplasma gondii* in which the adhesin MIC3 is inactivated by mutation.

Applicants note that the MIC3 protein encoded by the plasmid pMIC3i of Bassuny, which has been used to vaccinate mice, is not an inactivated protein. As specified in Bassuny on page 6223, left column, 2nd paragraph, this protein is the immature form of the MIC3 protein. Thus, this precursor will be processed co- or post-translationally to the mature form of MIC3. However, the present invention is directed to a mutant strain of *Toxoplasma gondii* comprising adhesin MIC1 and the adhesin MIC3 which have been inactivated. Accordingly, in the present invention adhesin MIC1 and adhesin MIC3 are not expressed or are expressed in a non-functional form, as specified in the application on page 6, lines 5-18. Applicants, respectfully point out that, the *Toxoplasma gondii* strain of the present invention is a mutant strain that is not

disclosed or suggested by Bassuny or Meissner. The cited references do not render the claimed invention obvious.

In summary, Bassuny does not teach or suggest an inactivated MIC3, as the immature form of the MIC3 is only a precursor of MIC3, which is processed to produce a mature, active MIC3, and Meissner et al. only discloses a MIC1 mutant strain. Consequently, there is no reason to combine the teachings of the cited references and to make the necessary changes to the teachings of the cited references to arrive at the claimed invention with a reasonable expectation of success.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should an interview be helpful to further prosecution of this application, the Examiner is invited to telephone the undersigned.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully Submitted,
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